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Introduction: There are several generic formulations of lamotrigine in Serbia that are widely used in the treatment of patients with epilepsy. The reduction of medical costs with use of generic formulations has potential risk because of the nature of disease, and it is necessary to investigate bioequivalence of each of generic formulations.

Aim: Comparison of the efficacy of the reference and generic formulation of lamotrigine and theinvestigation of lamotrigine serum concentrations variation. Date were compared with in vitro results of dissolution profiles of the reference and generic tablet formulation.

Patients (or Materials) and Methods: Lamotrigine steady-state concentrations were determined by high-performance liquid chromatography. In clinical study 16 patients participated, of whom 9 received reference formulation and 7 patients received generic formulation. Dissolution characteristics were evaluated at 3 points at physiologic pH range (pH 1.2, pH 4.5, pH 6.8), and difference ($f1$) and similarity ($f2$) tests were applied to dissolution data.

Results: The relationship between lamotrigine serum concentration (μg/mL) and lamotrigine dose (mg/kg/d) were linear in both formulations ($r^2 = 0.78484$ original and $r^2 = 0.83417$ generic). There are statistically significant lower lamotrigine serum concentrations in patient treated with original formulation (3.97 [4.1] μg/mL) than those in patients treated with generic formulations (5.78 [2.7] μg/mL). No dose-dependent adverse effects appeared in the patients, though patients treated with generic drug were receiving higher doses due to assumption that they are less potent. Brand drug had a lower standard deviation (SD) and data scattering because, as the dissolution data showed, it is less influenced by pH changes. Further dissolution profiles of 2 formulations were only similar in pH 1.2 medium.

Conclusion: Investigation showed equal efficacy of 2 lamotrigine formulations, and the variations in plasma concentrations are probably due to individual characteristics of patients and differences in liberation rate of drugs in 2 formulations. It can be claimed that even if there are differences in dissolution profiles of 2 drugs they can have equal therapeutic efficacy.

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Key words: lamotriginedissolution profilegeneric formulation

Disclosure of Interest: None declared.

PP214—TACROLIMUS BLOOD CONCENTRATION IN PATIENTS SUBJECTED TO RENAL TRANSPLANTATION: THE INFLUENCE OF GENDER

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Introduction: Tacrolimus, a potent immunosuppressant, is used for the prevention of allograft rejection in organ transplantation. Tacrolimus trough concentration (TTC) is still widely used as a guide to individualizing tacrolimus dose requirements in renal transplantation. The aim was to investigate the effect of patient's gender on TTC in renal transplant recipients on quaternary immunosuppressive therapy (tacrolimus, mycophenolate mofetil, prednisone, and anti–T lymphocyte globulin).

Patients (or Materials) and Methods: Present retrospective case series study involved 138 male and 70 female patients subjected to renal transplantation. The outpatient examination, recorded in the database of patients from year 2006 to 2008, as the unit of monitoring, contained such 3255 male and 1756 female examinations. Tacrolimus through concentrations were measured by fluorescence polarisation immunoassay (FPIA, TDx, Abbott Laboratories, Chicago, Illinois).

Results: Average TTC in outpatient examinations of male patients (7.098 [3.4870] ng/mL) were significantly higher ($t = 2.432$, $P = 0.015$) compared with female transplant recipients (6.852 [3.2726] ng/mL).In 25.3% of male examinations, TTC were within the "subtherapeutic" range (<5 ng/mL), while 28.3% of female examinations were within the same range; the difference was statistically significant. On the other hand, the number of examinations in which the TTC were "over the therapeutic" range (>10 ng/mL) in females were significantly lower than in males.

TTC (ng/mL)	Tacrolimus Trough Concentration (TTC); No. (%)		*P* value (Chi-square test)
	Male	Female	
<5	824 (25.3)	497 (28.3)	**0.0241**
5–10	1931 (59.3)	1028 (58.5)	0.6101
>10	500 (15.4)	231 (13.2)	**0.0386**
	3255 (100.0)	1756 (100.0)	

Conclusion: Our results indicated TTC as a useful guide in pointing out to potentially relevant influence of sex on its pharmacokinetics, what should be routinely considered and further studied.

Disclosure of Interest: None declared.

PP215—PHARMACOKINETIC STUDY OF GANCICLOVIR (GCV) AFTER SINGLE AND MULTIPLE DOSE IN HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) PATIENTS WITH CYTOMEGALOVIRUS (CMV) INFECTION

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Introduction: Pharmacokinetic data of GCV are limited in HSCT patients under preemptive therapy and its induced hematologic toxicity still problematic.The aim of this study was to evaluate the PK of GCV after single and multiple doses in HSCT patients with CMV infection and to identify correlation between PK parameters and hematologic toxicity.

Patients (or Materials) and Methods: A PK study was conducted between October 2008 and December 2009 at MG hospital in Beirut, after IV GCV treatment in HSCT recipients with CMV infection. CMV disease was recognized by the combination of clinical signs and antigenemia. Patients received 1-hour infusion of 5 mg/kg q 12h for 14 days, and a complete PK study was performed at days 1, 7, and 14. A compartmental and no PK analysis were performed, and plasma GCV was analyzed by an HPLC validated method with UV detection. An ANOVA analysis associated to Freadman test was performed to compare the mean PK parameters. The 95% CI was calculated for some parameters and $P < 0.05$ was considered significant.

Results: Twelve patients were enrolled in this study. A significant difference in creatinine clearance (Clcr) and trombecytopenia,

occurred between days 1, 7, and 14 ($P < 0.0001$, $P = 0.008$, respectively). Mean peak concentrations (C_{max}) was 9.4 (2.7) μ/mL (95% CI, 7.3–11.4) and decreased according to the bicompartmental model, without any significant accumulation during 14 days of treatment. Mean minimal concentration were well above the CI50 needed to inhibit human CMV. The plasma concentrations were not correlated with hematologic effects, indicating that the dosage of intracellular GCV is needed to explain this induced-toxicity. The mean half-life of elimination (t½β) was 6.4 (2) hours, and the total clearance of DHPG (CLGCV, 139 [20.4] mL/min) was greater and linearly correlated to CLcr ($r = 0.930$; $P < 0.0008$). The apparent volume of distribution (Vdβ) was (1.2 [0.32] L/kg) higher than that reported to the Solid Organ Transplant patients. At steady-state, an inter- and intra-patient variability were observed for CLGCV, t½β, and Vdβ suggesting the presence of a subgroup patient.

Conclusion: A population PK should be tested in the future studies to identify the best predictor parameter for dosage adjustment to improving the most efficacious GCV exposure.

Disclosure of Interest: None declared.